



# **Dietary Goals Towards Optimizing Women's Immune Systems with Emphasis on Palm- derived Phytonutrients, Phenolics and Fat-Soluble Antioxidants (carotenoids and Vitamin E)**

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# Paradox of Immune System Health Outcomes Disparity

- ▶ Occurrence of immune system diseases between women and men - WHY the persistence of this disparity?
- ▶ Stimulate ideas for future research to address and treat this disparity



# Women - disproportionate amount of auto-immune and immune dysfunction disease

- ▶ Long term area of mystery as to why there is such a gap in health outcomes
- ▶ In western countries both men *and* women tend to eat the same or similar diet that is too high in omega-6 EFAs and too low in omega-3 EFAs
- ▶ Yet same consumption of imbalanced, inflammation-provoking diet doesn't seem to impact the immune system the same way between females and males
- ▶ What to do about it
- ▶ Future research goals

# Human Evolution and Fat Consumption in the Diet

Then	Now
Lower Fat	Higher Fat
Lower Saturated Fat	Higher Saturated Fat
1:1 omega 6 : omega 3 EFAs	10:1 to 20:1 omega 6 : omega 3 EFAs

- ▶ The balance of omega-3 and omega-6 EFAs is *crucial* to immune system health

# Western diets deficient in omega-3 rich EFAs - inflammatory diet



- ▶ Omega-3 EFAs essential building blocks for cell membranes
- ▶ Diet is typical source for these mandatory nutrients
- ▶ Palm nutrients can play a key role in restoring balance to dietary intake of omega 3 EFAs

*...”Let your food be your medicine, and let your medicine be your food”...*

*Hippocrates*

# Women and Diet Patterns - Factors to Consider

- ▶ Observation - with respect to weight management and weight loss, women are more likely to try diets to achieve weight management goals, rather than exercise, over the course of a lifetime - gender-based difference
- ▶ Results in decreased fat consumption overall and unhealthy consumption of omega-6 fats in daily diet
- ▶ Excess weight and inflammation impact - increased benefit and greater need for omega 3 and omega 6 EFA balance
- ▶ Women more likely to restrict their calories, especially fats, at some point in their lifetime, as part of weight management or weight loss strategy
- ▶ Many women avoid fats of all kinds in their daily diet, including healthy fats, for a variety of reasons, including as a (popular misperception) way to avoid heart disease

# Women and Diet Patterns - Factors to Consider - More Research Needed

- ▶ Deprivation of healthy fats and their constituents (from palm - carotenoids, phenolics, tocotrienols, EFAs, etc.) may lead to unhealthy balance of essential fatty acids -or- not enough healthy fats in their personal nutrition; this could be the set-up for future immune-based problems
- ▶ ... Women may be *more* vulnerable to the absence of healthy fats in the diet, and that may be *part* of explaining *why* women experience immune system problems so much more frequently than men; this is such a complex area of investigation, rife with numerous signaling and feedback mechanisms that interact with and affect immune function, including cytokines and neurotransmitters - *more research needed*
- ▶ Women don't lose weight as readily as men - "physiological brakes" that seem to be in play for weight may also be tied to inflammation response and tied to dysfunctional immune system responses - *more research needed*

# Palm nutrients - fat-soluble and water-soluble

- ▶ TRF - tocotrienol-rich fraction
- ▶ Vitamin E - tocotrienols, tocopherols
- ▶ Carotenoids
- ▶ Phenolics





# Existing Research Points to Promising Outcomes for Immune Health - Further Investigation Needed

- ▶ Other factors that affect and mediate immune function include inflammatory markers such as the interleukins (Il-6, Il-8, etc.) and other cytokines that signal relative balance or imbalance in normal immune function
- ▶ The balance of omega-3 and omega-6 EFAs is crucial to immune system health
- ▶ Palm phytonutrients may:
  - ▶ Play an important role in immune function
  - ▶ Restore balance to the immune system - warrants more research attention and funding
- ▶ Both human and animal studies show beneficial immunoregulatory response to the consumption of tocopherols and tocotrienols, including research on women subjects

# Tocotrienol (TRF) supplementation and immune response in healthy females

- ▶ **STUDY (human):** TRF-rich (tocotrienol-rich fraction) supplementation w/ healthy female volunteers
  - ▶ Effects of supplementation with tocotrienol-rich fraction on immune response to tetanus toxoid immunization in normal healthy (female) volunteers.
    - ▶ assessment via TT (tetanus toxoid) vaccine challenge
    - ▶ interferon- $\gamma$  and interleukin (IL)-4 by the mitogen or TT-stimulated leukocytes increased, compared with the control group
    - ▶ produced significantly ( $P < 0.05$ ) lower amounts of IL-6 compared with the placebo group
    - ▶ authors conclusion: that TRF has immunostimulatory effects and potential clinical benefits to enhance immune response to vaccines.
    - ▶ What other benefits for improved or normalized immune response might be experienced from TRF supplementation? ***More research needed.***

# Carotenoids - Vitamin A supplementation effect on immune response in children

- ▶ **STUDY** (human): [Effect of vitamin A supplementation on immunoglobulin G subclass responses to tetanus toxoid in children.](#)
  - ▶ Randomized, double-masked, placebo-controlled clinical trial, the levels of the different anti-TT IgG subclasses were measured in 139 Indonesian preschool children (3 to 6 years of age) 2 weeks before and 3 weeks after immunization
  - ▶ Children who were given vitamin A prior to immunization had significant increases in IgG1 levels regardless of whether they were undergoing primary or memory reactions
- ▶ **Question** - With further research, can we determine whether *puberty* changes the incidence of immune system dysfunction and auto-immune diseases between females and males?

# Vitamin E supplementation and immune response in healthy elderly subjects

- ▶ **STUDY (human):** Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial.
  - ▶ To determine whether long-term supplementation with vitamin E enhances in vivo, clinically relevant measures of cell-mediated immunity in healthy elderly subjects.
  - ▶ **DESIGN:** Randomized, double-blind, placebo-controlled intervention study.
  - ▶ **SETTING AND PARTICIPANTS:** A total of 88 free-living, healthy subjects at least 65 years of age.
  - ▶ **INTERVENTION:** Subjects were randomly assigned to a placebo group or to groups consuming 60, 200, or 800 mg/d of vitamin E for 235 days.
  - ▶ **MAIN OUTCOME MEASURES:** Delayed-Type Hypersensitivity skin response (DTH); antibody response to hepatitis B, tetanus and diphtheria, and pneumococcal vaccines; and autoantibodies to DNA and thyroglobulin were assessed before and after supplementation.

# Vitamin E supplementation and immune response in healthy elderly subjects (cont'd)

- ▶ **RESULTS:** Supplementation with vitamin E for 4 months improved certain clinically relevant indexes of cell-mediated immunity in healthy elderly. Subjects consuming 200 mg/d of vitamin E had a 65% increase in DTH and a 6-fold increase in antibody titer to hepatitis B compared with placebo (17% and 3-fold, respectively), 60-mg/d (41% and 3-fold, respectively), and 800-mg/d (49% and 2.5-fold, respectively) groups. The 200-mg/d group also had a significant increase in antibody titer to tetanus vaccine. Subjects in the upper tertile of serum alpha-tocopherol (vitamin E) concentration (>48.4 micromol/L [2.08 mg/dL]) after supplementation had higher antibody response to hepatitis B and DTH. Vitamin E supplementation had no effect on antibody titer to diphtheria and did not affect immunoglobulin levels or levels of T and B cells. No significant effect of vitamin E supplementation on autoantibody levels was observed.

# Vitamin E supplementation and immune response in healthy elderly subjects (cont'd)

- ▶ **CONCLUSIONS:** Our results indicate that a level of vitamin E greater than currently recommended enhances certain clinically relevant in vivo indexes of T-cell-mediated function in healthy elderly persons. No adverse effects were observed with vitamin E supplementation.
- ▶ This warrants further investigation, in elderly subjects in general, and in female elderly subjects in particular, given that women tend to outlive men by 10 years on average.
- ▶ Interesting that some aspects of immunity were positively impacted by the vitamin E supplementation while others were not affected.

# Animal studies

- ▶ **STUDY - Vitamin E, 3 forms (murine / mice): Supplementation with natural forms of vitamin E augments antigen-specific TH1-type immune response to tetanus toxoid.**
  - ▶ This study compared the ability of three forms of vitamin E [tocotrienol-rich fraction (TRF), alpha-tocopherol ( $\alpha$ -T), and delta-tocotrienol ( $\delta$ -T3)] to enhance immune response to tetanus toxoid (TT) immunisation in a mouse model. The results of this study showed that delta-tocotrienol ( $\delta$ -T3)] enhanced immune response to tetanus toxoid (TT) immunisation in a mouse model the most, followed by tocotrienol-rich fraction (TRF), and then alpha-tocopherol ( $\alpha$ -T).
  - ▶ The production of IFN- $\gamma$  and IL-4 by splenocytes from the vitamin E treated mice was significantly ( $P < 0.05$ ) higher than that from controls. The IFN- $\gamma$  production was the highest in animals supplemented with  $\delta$ -T3 followed by TRF and finally  $\alpha$ -T. *Production of TNF- $\alpha$  was suppressed in the vitamin E treated group compared to vehicle-supplemented controls.* Supplementation with  $\delta$ -T3 or TRF can enhance immune response to TT immunisation and production of cytokines that promote cell-mediated (TH1) immune response.

# Animal studies (cont'd)

- ▶ **STUDY - Tocopherols and tocotrienols (murine / rats): Dietary effect of tocopherols and tocotrienols on the immune function of spleen and mesenteric lymph node lymphocytes in Brown Norway rats.**
  - ▶ Immunoregulatory effects of dietary alpha-tocopherol (Toc) and tocotrienols (T-3) on humoral and cell-mediated immunity and cytokine productions were examined
  - ▶ In Brown Norway rats. We found that the IgA and IgG productivity of spleen and mesenteric lymph node (MLN) lymphocytes was significantly enhanced in the rats fed on Toc or T-3, irrespective of concanavalin A (Con A) stimulation of the lymphocytes. On the contrary, the IgE productivity of lymphocytes from the rats fed on Toc or T-3 was less without Con A stimulation, but was greater in the presence of Con A, especially in the T-3 group. Toc or T-3 feeding significantly decreased the proportion of CD4+ T cells and the ratio of CD4+/CD8+ in both spleen and MLN lymphocytes of the rats fed on Toc or T-3. These results suggest that oral administration of Toc and T-3 affects the proliferation and function of spleen and MLN lymphocytes.

Increased IgA and IgG productivity of spleen and mesenteric lymph node (MLN) lymphocytes on Toc or T-3

Decreasing production of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )

Higher interferon-gamma productivity of MLN lymphocytes



# Animal studies (cont'd)

- ▶ **STUDY - phenolics (murine / mice): Gene expression changes in spleens and livers of tumour-bearing mice suggest delayed inflammation and attenuated cachexia in response to oil palm phenolics.**
  - ▶ Oil palm phenolics (OPP) previously showed anti-tumour activities in vivo via a cytostatic mechanism at 1,500 ppm gallic acid equivalent. Here, we report other possible molecular mechanisms by which this extract attenuates cancer, especially those concerning the immune response.
  - ▶ **CONCLUSIONS:**
  - ▶ Inflammatory genes were downregulated through time, further suggesting attenuation of systemic inflammation and cachexia. These effects correlated with the delayed in vivo development of syngeneic tumours in mice given OPP.
  - ▶ **This study suggests the possible utilization of OPP as an anti-tumor and anti-cachexia agent.**

# Women's Health and Immune System Function - Future Research Focus Areas

- ▶ Establishing whether there is consistently improved resistance to oxidative damage to the immune system with the added consumption of palm and supplementation of palm phytonutrients - changes in tumor growth, markers, etc.
- ▶ Research impact of all palm nutrients on auto-immune illnesses that are more common in women, especially Rheumatoid Arthritis (RA) - dosages and outcomes, any titration or dose-dependent responses?
- ▶ Women who regularly eat healthy fats, including palm oil supplements, and their immune system health outcomes over time, compared to women who don't consume healthy fats and palm oil supplements
- ▶ Women who avoid fat in the diet compared to women who enrich their diet with specific palm derived phytonutrients
  - ▶ Carotenoids
  - ▶ Vitamin E
  - ▶ Tocotrienols - delta
  - ▶ Tocopherols
  - ▶ Phenolics - antioxidant properties and more

# Women's Health and Immune System Function - Future Research Focus Areas (cont'd)

- ▶ Women whose diet contains plenty of palm oil - lower incidence of immune system diseases, compared to women whose diet consists of no palm or its nutrients
- ▶ Women who consume phenolics or tocotrienols or tocopherols or carotenoids or palm as a supplement, not necessarily cook with palm oil and their health outcomes w/ emphasis on immune system
- ▶ Women who consume vitamin E and its fractions (tocotrienols or tocopherols) and their immune system status over time - healing or health promoting phytonutrient...
- ▶ Women and all of these studies done across the spectrum of women's reproductive life cycle stages - there may be some variability tied to endocrine system
- ▶ Women, palm oil and its derivatives, studied in conjunction with thyroid function, and other aspects of metabolic wellness

# Women and Dietary Fat Needs for a Lifetime

- ▶ Overall balance of dietary intake of omega 3 and omega 6 fats

- ▶ **Seafood - Fish and Shellfish**

- ▶ Halibut
- ▶ Herring
- ▶ Mackerel
- ▶ Oysters
- ▶ Salmon
- ▶ Sardines
- ▶ Trout
- ▶ Tuna
- ▶ Shrimp

- ▶ **Nuts**

- ▶ Especially walnuts

- ▶ **Seeds**

- ▶ **Oils**

- ▶ Palm oil
- ▶ Cod liver oil
- ▶ Flaxseed oil
- ▶ Mustard oil
- ▶ Walnut oil

- ▶ **Vegetables**

- ▶ Brussels sprouts
- ▶ Kale
- ▶ Mint
- ▶ Parsley
- ▶ Spinach
- ▶ Watercress
- ▶ Cauliflower



# Thank You for Your Time and Attention

Questions welcome.

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